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REVIEW ARTICLE

A Review of Approaches for the Management of Specialty Pharmaceuticals in the United States

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Abstract With increased innovation and development of specialty pharmaceuticals, the US and global healthcare industries are looking to implement appropriate management strategies to control both utilization and costs. Specialty pharmaceuticals are high-cost medications that treat complex, chronic, rare, and difficult-to-manage conditions. These drugs require special drug handling, appropriate clinical outcomes monitoring, and effective cost controls. The primary scope of this article is to discuss various strategies being implemented for specialty pharmaceutical utilization and cost management and correlated outcomes in the USA; these outcomes include enhanced health insurance plan benefit designs with formulary modifications and greater patient cost burden. Additional methods to manage specialty pharmaceuticals include the use of specialty pharmacies for drug distribution, increased emphasis on coordination of care and evidence-based medicine, as well as healthcare reform and regulations. Healthcare spending, both in the US and globally, continues to increase, with a rising proportion of drug spend towards specialty pharmaceuticals. Continued specialty pharmaceutical innovation and introduction of biosimilar products will evolve the currently utilized management strategies for these drugs.

Key Points for Decision Makers

Cost drivers for increased drug spend on specialty pharmaceuticals include increased utilization, expanded indications, and the introduction and development of new biologic agents.

Key management strategies for specialty pharmaceuticals include the implementation of specialty tiers and complex formulary designs, drug restrictions through prior authorizations and quantity limits, co-payments and co-insurance rates that increase patient cost burden, specialty pharmacy provider use for drug distribution, medication therapy management programs to increase coordination of care, quality measures enforced through healthcare reform and accountable care organizations, increased use of evidence-based medicine, and government regulation for biosimilars and price controls.

Continued development of specialty pharmaceuticals in the biopharmaceutical industry pipeline, primarily targeting orphan diseases, oncology, hepatitis C, inflammatory conditions, multiple sclerosis, and HIV, coupled with the introduction of biosimilars, will affect the cost impact of these drugs and evolve drug utilization and cost-management strategies.

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1 Background on Specialty Pharmaceuticals

1.1 Definition of Specialty Pharmaceuticals

The development and utilization of specialty pharmaceuticals have significantly impacted global healthcare

practices and costs. Although the development of, and healthcare spending on, specialty pharmaceuticals has increased over the last decade, a universally accepted definition remains undetermined. Characteristically, a specialty pharmaceutical treats a complex, chronic, rare, and difficult-to-manage condition and may include blood derivatives or bioengineered proteins. Administration of specialty drugs is typically via injection or infusion in the physician's office or via self-injection; however, some specialty drugs may be orally administered. These biopharmaceutical drugs may require special handling, such as refrigeration or radiation shielding and typically need ongoing monitoring for efficacy, safety, and an overall positive clinical response [1, 2]. According to the 2010 Healthcare Distribution Management Association (HDMA) study of specialty pharmaceutical distributors, on average, specialty drugs account for 49 % of all pharmaceuticals that necessitate risk evaluation and mitigation strategies (REMS) [3]. Specialty pharmaceuticals are often high-cost prescription drugs, ranging from several hundred to thousands of dollars, with some regimens costing up to $US10,000 per month [1, 3–5]. For example, according to the Centers for Medicare and Medicaid Service (CMS) Part D drug benefit, a specialty drug is categorized as one with a minimum monthly cost of $US600. Some insurance plans also set cost thresholds, which can be up to double this amount. Through survey information, 84 % of commercial payers classify a specialty pharmaceutical based on the cost, with $US1,154 determined as the average minimum monthly cost [1]. The term 'specialty pharmaceuticals' is sometimes used interchangeably with 'biologic drugs'; however, it is important to note that not all specialty drugs are biologic products (e.g. sofosbuvir, a small molecule for hepatis C) and not all biologic products are considered specialty drugs (e.g. insulin) [4, 5].

1.2 Scope and Cost of Specialty Drugs

For the scope of this review article, case examples and outcomes from specialty pharmaceutical utilization strategies aimed to reduce cost are focused primarily in the US due to the diversity and complexities across its health system. A subsequent review focusing on non-US approaches when there is greater governmental involvement as a payer rather than diverse private and public insurance plans would be warranted since the rising costs of specialty drugs is a global problem. Some examples are presented from EU data, particularly related to the application of cost-effectiveness analysis and biosimilar prescribing since there is more information from the EU in these endeavors.

Overall US healthcare spending, which encompasses hospitalizations, physician office visits, and prescriptions filled, continues to rise. Approximately 11 % of healthcare costs are related to prescription medications [6, 7]. In the USA in 2013, prescription drug expenditure was $US329.2 billion. Spending for specialty drugs and biologic medications has increased more significantly than the spending for traditional small molecules. In 2013, specialty medications in the retail, mail, and non-retail (i.e., long-term care, institutional) settings accounted for 29 % of spending on medicines. Spending on biologics increased 9.6–28 %, whereas the spending for small molecules increased by 0.1 %, accounting for 72 % of drug expenditure [8–10]. Five of the top ten drugs by US sales in 2013 are specialty drugs. They account for sales in excess of $US21.1 billion. Four of these drugs are indicated for inflammatory conditions; one for supportive care of malignancies [11]. Inflammatory diseases, multiple sclerosis (MS), and oncology care accounted for 60 % of the spending on specialty drugs [12]. From 2012 data, commercial health plans exhausted more than 90 % of their total specialty drug spend on approximately 5 % of enrollees. However, the total specialty drug spend is only 11–12 % of total drug spending, which accounts for approximately 20–24 % of overall commercial health plan spending [13].

Global medication sales are expected to exceed $US1 trillion in 2014. The impact of rising costs of specialty drugs is a global concern. Over the next 5 years, spending on traditional pharmaceuticals is expected to increase only 5 % in major markets, whereas it is estimated to increase 69 % in emerging markets primarily due to the burden of chronic disease and higher volume demand for small-molecule medicines. Through 2017, the developed countries are estimated to have a 30 % increase in specialty pharmaceutical spend compared with a 90 % increase in emerging markets. The emerging markets currently have a much lower baseline since these markets are not as highly penetrated, with decreased access and affordability for specialty pharmaceuticals [9, 10].

Through 2018, a total of 39 specialty products will face patent expirations, creating opportunities for $US13.1 billion in specialty generic drugs. Additionally, through 2010, a total of 51 biologic products will encounter patent expirations, leading to a potential $US31.8 billion market for biosimilars.

In 2013 alone, 36 new molecular entities (NMEs) were brought to market, including ten cancer drugs and 17 orphan drugs; of these 36 entities, 20 were specialty drugs [9]. Additional drug development is expected from a robust specialty pipeline, with numerous expected launches over the next 5 years. Of this drug pipeline, approximately 36% are focused on orphan diseases, 17 % on oncology, 14 % on hepatitis C, 13 % on inflammatory conditions, 11 % on other conditions, 5 % on MS, and 4 % on HIV [10]. New innovative products frequently lead to greater utilization

and expense. For example, Gilead's sofosbuvir (Sovaldi™) for hepatitis C costs $US84,000 for a curative 12-week course of treatment. Reported first quarter sales for 2014 were $US2.3 billion [14].

2 Cost and Utilization Strategies for Specialty Pharmaceuticals in the USA

2.1 Benefit Design Modifications

Specialty pharmaceutical management should balance the need for innovative therapies while employing enhanced benefit design strategies to control unsustainable rising costs of specialty drugs [1]. This paper will review some strategies that have been employed to control these healthcare costs. With new health insurance plan benefit structures, there has been a shift to an increased cost burden for patients.

2.1.1 Formulary Modifications, Prior Authorization, Quantity Limits

Both US Government and commercial insurance plans are modifying benefit designs to better ensure appropriate medication utilization and cost control. Since 2005, CMS required formularies to include "all or substantially all" drugs from six protected classes of clinical concern: anticonvulsants, antidepressants, antineoplastics, antipsychotics, antiretrovirals, and immunosuppressants for the treatment of transplant rejection. On 6 January 2012, CMS proposed a rule with aims of reducing costs and protecting patients from over-utilization that would significantly impact Medicare beneficiaries. The ruling would have removed protection for antidepressant and immunosuppressant treatments starting in 2015 and remove antipsychotic therapies 1 year later. However, CMS withdrew its proposal due to vocal opposition [15].

Furthermore, in order to contain costs and maintain appropriate utilization, Medicare formularies are implementing prior authorizations (PAs), especially on high-cost biologic agents. PAs require the prescriber to obtain preapproval based on the terms set by the pharmacy benefit plan, which are determined based on clinical need and therapeutic rationale [16, 17]. Based on data collected from stand-alone and Medicare Advantage prescription drug plans, biologic medications with greater coverage and within a tier of higher cost sharing, such as anemia or rheumatoid arthritis, were more likely to be associated with a prior authorization than those on lower cost-sharing tiers, such as diabetes or oncology drugs [16]. Authorization techniques may be implemented to limit access to selected innovative therapies, since many specialty pharmaceuticals modulate a specific targeted protein and will only benefit a subset of patients [1].

Due to the development of new therapies for MS, patients have expanded therapeutic options. Managed care organizations (MCOs) are using varied strategies to manage utilization and costs. For example, 58 % of 109 MCOs surveyed implement prior authorizations for MS specialty therapies. However, use of this strategy may decrease, since there is little risk of MS medications being abused. Instead of PAs, several companies are restricting quantity limits and using restricted pharmacy networks to prevent inappropriate use. Frequently, 14- to 30-day supply limits are implemented for many specialty drugs in all therapy classes, despite that they are used to treat chronic conditions. Limiting the maximum amount that can be dispensed to a patient may reduce costs and minimize waste if doses or treatment regimens are changed [14]. Unfortunately, these policies may adversely impact patient out-of-pocket (OOP) expenditures due to co-pays and co-insurance [18].

2.1.2 Complex Formulary Tiers—Co-Payments vs. Co-Insurance

Cost-containment mechanisms include cost sharing that increases overall OOP costs for patients. These techniques involve mandated co-insurance and/or co-payments. The formulary tier determines the varying costs for co-payments and co-insurance. Co-pays can be set as flat rates for all specialty drugs or set based on tiers of preferred and non-preferred therapeutic agents, while co-insurance is a defined percentage [2].

Medicare formularies have looked to create tier structures that are more complex than the two-tier framework with generic medications on tier 1 and brand medications on tier 2, and shift a greater cost burden for the patients through increased cost sharing. This approach is used to gear providers and patients towards lower cost drugs. Under Medicare Part D, CMS has designated only one tier as a specialty tier. Cost sharing in this tier is limited to a 25 % maximum after the deductible and before the initial coverage limit, or limited to 33 % in plans with decreased or no deductible under alternative prescription drug coverage designs. The specialty tier is for Part D drugs exceeding the payer's negotiated prices of $US600 per month. The implementation of a specialty tier allows for lower cost sharing on non-specialty tiers [19].

According to the Kaiser Family Foundation data, the table below represents the increase in Medicare Part D Plans (PDPs) that use specialty tiers from 2010 to 2013 [20].

	2010	2011	2012	2013
Percentage of plans with a specialty tier	84 %	85 %	87 %	90 %
Average number of drugs on a designated specialty tier	158	171	179	194
Average percentage of drugs on a designated specialty tier	4.8 % of all Part D drugs	6.4 %	7.8 %	8.6 %

Most top-selling biologics for stand-alone and Medicare advantage prescription drug plans are on the fourth tier, which requires the highest level of cost sharing compared with diabetes medications (i.e., insulin), which are typically on tiers two or three. For these biologics, co-payments can reach up to $US60 for a 30-day supply, and co-insurance is typically 25 % of the drug's cost, which increases the patient cost burden for these high-cost medications. However, data from 2006 to 2009 reveal that the most common co-insurance rate for biologic agents is 33 %, which is an even greater patient cost burden [16, 20].

Commercial health plans in the US typically use a three-tier benefit structure, with 77 % of covered workers in plans that have three or more tiers of various cost-sharing levels. These tiers are designed such that generic drugs are on the first tier, preferred branded drugs are on the second tier, non-preferred branded drugs are on the third tier, and fourth-tier drugs include biologics, specialty pharmaceuticals, and lifestyle drugs. The differentiation between tier 2 and 3 products is based on relative safety, effectiveness, and cost as determined by the pharmacy benefit plan for branded drugs without generic substitutes. Three or more tiers of cost sharing have been implemented more frequently over the past 10 years, with more commercial plans utilizing co-payments, faced by 55 % of employees, compared with co-insurance applied to 36 % of employees. The typical co-payment amounts are comparable from 2011 to 2012 at $US10 for first-tier drugs, $US29 for second-tier drugs, $US51 for third-tier drugs, and $US79 for fourth-tier drugs. On the other hand, for employees covered by a commercial plan with more than three tiers who face co-insurance versus co-payments, the typical average co-insurance levels are 20 % for first-tier drugs, 26 % for second-tier drugs, 39 % for third-tier drugs, and 32 % for fourth-tier drugs. Only 10 % of employees have their prescription drug benefit through commercial plans with two tiers, with an average co-payment of $US11 for first-tier drugs and $US29 for second-tier drugs. For two-tier plans with co-insurance requirements, the average co-insurance is 27 % for their second-tier drugs. Only 6 % of workers have a plan where cost sharing is identical regardless of the drug, with an average $US13 co-payment faced by 14 % of this population, and an average 22 % co-insurance faced by 85 % of this population. A majority of commercial plans, covering 87 % of workers, limit employees' cost sharing with varying OOP maximums. For example, 41 % of plans have a $US3,000 or higher OOP maximum, whereas 16 % of plans have a maximum OOP payment of $US1,500 or less [13].

There is also an increased demand for patient assistance programs (PAPs) established by pharmaceutical and biopharmaceutical manufacturers, which provide no- or low-cost medications to those with no insurance or those that are under-insured. The US Federal Government does not require PAPs, but manufacturer companies do receive significant tax breaks. PAPs increase access to medications for individuals who cannot afford these high-cost medications [21]. By 2016, an estimated $US180–190 billion (i.e., 15–16 %) savings for patients, payers, drug wholesalers, and distributors will be achieved through discounts and rebates on brand name medications [8].

2.2 Drug Distribution Networks and Channels

2.2.1 Specialty Pharmacies

Specialty pharmacies combine medication dispensing with clinical disease management. Their services have been used to improve patient outcomes and contain costs of specialty pharmaceuticals [4]. These may be part of independent pharmacy businesses, retail pharmacy chains, wholesalers, pharmacy benefit managers (PBMs), or health insurance companies. Over the last several years, payers have been transitioning to obligate beneficiaries to receive self-administered agents (SAAs) from contracted specialty pharmacies, limiting the choice of acceptable specialty pharmacy providers (SPPs) for patient services [3, 19, 22].

Benefits from more restricted specialty networks include more cost-effective pricing and less variability in patient care and experience [3, 4]. Specialty pharmacies manage the complex reimbursement process, with the goal of making it easier for patients, providers, and payers. PBMs can reject filling or covering a specialty pharmaceutical product if is it not dispensed through its preferred SPP. These entities provide cost-management services, including contracting with pharmaceutical manufacturers for discounted pricing and assisting patients to obtain PAs [4]. Payer organizations can receive medication rebates directly through contracting with specific specialty vendors or through PBMs. These rebates create cost savings and are typically available for specialty pharmaceutical classes with higher utilization, such as those agents for rheumatoid arthritis and MS as well as growth hormones [3, 23]. Specialty pharmacies also help payers control drug costs by only providing medications for individuals who meet regulated indications for these high-cost drugs [21].

Additional clinical services include educating patients and their caregivers about drug administration and handling, as well as monitoring for potential adverse effects, drug interactions, and patient adherence. However, there is also some concern about fragmented care, since the specialty pharmacy may not be part of a multidisciplinary team within the clinical care setting with access to relevant patient information. An increased use of electronic health records may mitigate this issue. Specialty pharmacies also frequently have mechanisms to provide refill reminders and clinical status follow-ups. Specialty pharmacies frequently provide mail-order home delivery; some offer distribution via community pharmacies [24].

The National Comprehensive Cancer Network (NCCN) Task Force expressed concern for the integrity of medications that require sterile compounding by the pharmacists and subsequent delivery to the patient or physician. With these distribution mechanisms, it is difficult to verify the chain of custody and appropriate storage of the compounded medications. Hematologic, renal, and hepatic function are frequently tested immediately prior to drug administration in oncology clinics. If the medication has been prepared by the compounding pharmacy prior to test results being reported, cancellation of treatment or dose modification based on these laboratory tests may result in waste. Thus, unused compounded medication may mean that a mechanism designed to control costs may adversely impact potential savings. Health system pharmacies (i.e., inpatient hospital pharmacies and outpatient clinic pharmacies) are also disturbed by the loss of revenue with the specialty pharmacy distribution model, since the health system will receive reimbursement for administration of the product, but not for dispensing of the product itself [24, 25].

2.3 Medication Therapy Management and Coordination of Care

Legislation in the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 mandated to provide medication therapy management (MTM) services for individuals with multiple chronic diseases who are taking multiple medications. According to CMS guidance documents for 2013, reimbursable MTM services provided by Medicare Part D sponsors must meet the following conditions for beneficiaries: (1) a minimum of two or three chronic disease states, (2) taking a minimum of two to eight medications, and (3) likely to incur ≥$US3,144 in annual costs for Part D drugs [26].

Several publications document MTM services in oncology. MTM services correlate to improvements in patients' understanding of medication indications, therapeutic goals, and appropriate and safe medication use by identifying patient-specific drug-related problems (DRPs). Pharmacists play a critical role with direct patient interactions, coordinating care, and ensuring accurate prescribing and dispensing practices through implementation of health information technology (HIT) improvements, such as electronic order-entry systems [25, 27]. Large oncology practices, which constitute about 40 % of US oncologists, are increasingly looking to incorporate oncology pharmacists to ensure protocol compliance, accurate dose adjustments, a heightened level of awareness for drug–drug interactions, and opportunities for cost savings. For example, by employing an oncology pharmacist and pharmacy technician, oncology centers have been able to prepare and administer intravenous immunoglobulin (IVIG) doses at the center compared with costs of $US1,000 for purchasing ready-to-administer IVIG or sending patients to an outpatient hospital setting [28, 29]. Additional opportunities for cost savings by employing an oncology pharmacist include accurate tracking of medication use and maintenance of inventory. Oncology pharmacists also work closely with patients to provide medication refills and appropriate medication counseling, as well as assisting patients with obtaining free or low-cost medications and taking advantage of patient-assistance programs typically offered through drug manufacturers. Pharmacist MTM services are reimbursable through Current Procedural Terminology (CPT) codes identified by Medicare Part D [29].

Implementation of specialty pharmacy centers and MTM practices to improve medication adherence, reduce adherence barriers, create personalized care plans, and implement cost-savings mechanisms are crucial to not only the field of oncology, but also other disease states treated with specialty drugs, such as MS and HIV. In a study assessing the effectiveness of specialty pharmacy management services on patient adherence to MS medications, medication adherence for the study population was approximately 60 % compared with 2011 drug trend data showing a 33 % adherence rate to MS therapy. The adherent group in this study had fewer MS-related emergency room visits and lower medical costs than the non-adherent group [30]. Studies of pharmacist MTM programs in both community pharmacy and HIV specialty practice settings have demonstrated improved patient adherence, with significantly better patient outcomes, such as reduced viral loads and rising CD4+ T-lymphocyte counts [30–33]. However, the total mean annual healthcare cost per patient was 10 % higher for patients using the MTM community pharmacy services. This was related to additional use of non-HIV antiretroviral therapies (ART) and mental health medical care [33]. Long-term benefits were not evaluated in these studies.

Health institutions and payers are also developing positions for clinical specialists to implement and monitor

appropriate clinical drug use, correlating to optimization of drug spend. Advocate Physicians Partners (APP) is a part of the Advocate Health System across Chicago and central Illinois, and is characterized as a hybrid model comprising a physician health organization (PHO), MCO, and an accountable care organization (ACO). In order to control pharmacy expenditure and ensure the adherence to evidence-based protocols that have increased less than 3 % in per-member-per-month (PMPM) expenses over 2012, APP created an oncology clinical pharmacist position. This clinical pharmacist was responsible for maintaining specialty/oncology-related protocols, measuring and promoting compliance with protocols, and developing tools and educational resources for physicians, staff, and patients. Incorporated into clinical pathway protocols were PAs, where the physicians needed to identify the indication for drug use prior to approval, dispensing, and administration of the drug. To enhance protocol compliance, the oncology clinical pharmacist created communication programs targeting under-compliance with protocols specifically targeting the staff with under-utilization of designated protocols. A protocol compliance report was generated quarterly. Prior to this implementation, the protocol compliance was 62 %. However, after the clinical pharmacist implemented programs to educate physicians and nurses about the appropriate clinical and economic outcomes associated with protocol compliance, the value increased to 100 %. Physicians were now notifying the pharmacy of appropriate indications for specific medication utilization compared with general chemotherapy protocols that were previously being used. Due to clinical pharmacist interventions and increased protocol compliance by physicians, the organization benefited from enhanced clinical education and improved medication utilizations related to diagnoses, thus minimizing an increase in drug expenditures [34].

2.4 Accountable Care Organizations

ACOs have been implemented across the US as part of healthcare reform through the Patient Protection and Affordable Care Act (PPACA) of 2010. The ACO model creates a new healthcare delivery and payment model focused on value-based pricing and reimbursement as well as on expanding the bundling of payments and use of medical homes. Healthcare reform aims to improve quality and efficiency of care, particularly at the current time where overall healthcare costs account for 23 % of the US federal budget. With ACOs paying closer attention to the cost of care, there will be greater scrutiny to determine coverage of specialty pharmaceuticals due to their high acquisition costs. For shared savings reimbursement from CMS, Medicare ACOs must meet certain thresholds for 33 quality standards that aim to provide better care for individuals and better health for populations. Shared savings and losses through CMS are determined based on the difference between fee-for-service spending for a defined year for the covered population of an ACO and a risk-adjusted benchmark determined by estimated Medicare Part A and Part B expenditures that would have occurred without the ACO in place. The risk-adjusted benchmark is estimated based on Part A and Part B spending historically over the previous 3 years. Based on these incentives for improving quality of care, while also reducing costs, it may impact the choice of preferred specialty pharmaceuticals. ACOs are assessing the overall value and benefit of therapeutic interventions to patient outcomes, both clinically and financially, in order to provide coverage for high-cost specialty drugs when medically appropriate. According to two established ACO models, Geisinger Health System and Kaiser Permanente, success has been achieved by linking patient care to gatekeeper physicians within an organization in addition to incentives that reward cost-effective, conscientious, and timely care. After more experience and release of data for the ACO model in regards to cost-effective utilization of specialty pharmaceuticals, future management strategies may have a significant impact for these high-cost medications [35].

2.5 Evidence-Based Medicine

The use of comparative effectiveness reviews has also increased, and involves a population-based analysis to help determine and assess evidence linked to the effectiveness, benefits, and harms of different treatment options. This heightened focus over the last several years is supported by the US federal implementation of the Patient-Centered Outcomes Research Institute (PCORI), which was created by the PPACA of 2010. The PPACA launch of the PCORI establishes an organization aimed at providing the best obtainable evidence to optimize healthcare decisions and outcomes. PCORI provides several opportunities for research funding, which can support effectiveness research of specialty pharmaceuticals, which can be quite difficult and costly, especially when comparing outcomes between agents. The use of comparative effectiveness research (CER) by health insurance plans has increased over the last several years. Medicare Part D and commercial plans may consider CER, but it is not permitted to be utilized by Medicare Part B. The use of CER and other outcomes-based research studies have allowed companies to implement more appropriate cost-control mechanisms compared with only utilizing clinical efficacy and safety data for medications. The application and value of CER and outcomes-based research will increase over the next several years [4, 8].

Many countries use CER in their decision making. Some examples of agencies that provide guidance regarding use of drugs and devices are the National Institute for Health and Care Excellence (NICE) in the UK, the Haute Authorite de Sante (HAS) in France, the Pharmaceutical Benefits Scheme (PBS) in Australia, and the Institut fur Qualitat und Wirtschaftlichkeit im Gesundheitswesen (IQWiG) in Germany [36]. In addition to evaluating clinical-effectiveness data, consideration of cost-effectiveness analysis and budgetary impacts are part of these agencies' mandates. Every National Health Service (NHS) patient in the UK has the right to NICE-recommended therapies, although access to the required companion molecular diagnostic testing and lack of referrals to experts limits the use of the approved treatments [37]. Since 2007, NICE has recommended 31 % of the new medications it has reviewed. Within the field of oncology, NICE recommended, with no or minor restrictions, 52 % of therapies it reviewed over its first 10 years of operations (1999–2008) [38]. Rejection rates for oncology therapies have risen to 65 % since 2009. Cost effectiveness has been the most frequent reason for rejection. NICE considers a cost of £30,000 to be satisfactory for each quality-adjusted life-year (QALY), a measure of disease-burden that takes into account both the quality and the quantity of life. The proposed pricing structure of some rejected medications can be reconsidered in order to obtain NICE endorsement. In addition, the UK has a temporary Cancer Drug Fund of £200 million per annum to provide access for patients who need treatment for their malignancies with NICE-rejected therapies. This fund is set to expire in 2016 [39, 40].

2.6 Role of Biosimilars

The Biologics Price Competition and Innovation Act (BPCIA) of 2009 authorized the US FDA to provide an approval pathway for biologics that are 'biosimilar' to a reference product while providing 12 years of market exclusivity for the original branded biologic product. The BPCIA also provides for potential of 'interchangeability.' Biosimilarity is defined as the product being "highly similar to the reference product notwithstanding minor differences in clinically inactive components." Interchangeability is a higher standard. It is defined as the product being able to "produce the same clinical result as the reference product in any given patient and, if the biological product is administered more than once to an individual, the risk in terms of safety or diminished efficacy or alternating or switching between the use of the biological product and the reference product is not greater than the risk of using the reference product without such alteration or switch" [41]. This bill allows a pharmacist to make substitutions of products with similar reference therapeutic products as designated by the FDA. The FDA published draft guidance providing direction on scientific and quality considerations to demonstrate biosimilarity and addresses questions in relation to the BPCIA [42].

Lessons can be learned from the uptake of biosimilars in Europe. The EU introduced biosimilar legislation in 2004 along with the European Medicines Agency (EMA) issuing a class-specific guidance for several traditional and specialty pharmaceuticals: insulin, human growth hormone (HGH), granulocyte colony-stimulating factors (G-CSFs), erythropoietins, interferons, low-molecular-weight heparins, monoclonal antibodies (mAbs). European biosimilars became available in 2007. Sixteen biosimilar products were approved in the EU for HGH and growth factors [43]. In July 2013, The EMA's Committee for Medicinal Products for Human Use (CHMP) recommended marketing authorizations for the first two mAb biosimilars. Remsima™ and Inflectra™ were deemed similar to the reference product, infliximab (Remicade™), a chimeric mAb [44]. No significant safety issues have been attributed to biosimilars for EU products. However, the EMA advised against an automatic substitution policy, and the agency requires biosimilar manufacturers to implement risk management programs (RMPs). This RMP requirement may provide mixed messages to physicians about potential safety issues [45]. Uptake for biosimilar prescribing has been relatively slow in Europe despite price reductions of 14–35 % relative to the originator's prices due to the reluctance of physicians for biosimilar prescribing [46]. Nevertheless, European sales of one product, Zarzio™, a biosimilar filgrastim product, have exceeded those of the reference product, Neupogen™ [47]. Cost-effectiveness has been demonstrated for Zarzio™ for prophylaxis or treatment of febrile neutropenia compared to Neupogen™ and its long-acting counterpart, pegfilgrastim (Neulasta®), across five European countries [48]. If there were a significant shift toward greater use of biosimilar products, as patents for biologic products with global sales of $US100 billion expire by 2020, substantial savings would be available for patients and payers. However, it is unrealistic to project a change in market share similar to that seen with small-molecule generic products [49].

2.7 Government Pricing Controls

There is limited uptake of government pricing controls for pharmaceuticals and biopharmaceuticals in the US compared to the EU, primarily due to differences in the funding and structure of the healthcare systems. On 4 February 2013, the Patient's Access to Treatment Act (PATA) of 2013 was introduced in the House of Representatives with the plan to limit cost sharing of specialty tier drugs to the level of non-preferred brand tiers. If plans have more than

one non-preferred tier, the specialty tier drug's cost sharing will be limited to the tier with lower cost sharing for enrollees. Additionally, this proposed law would require no more than a 10 % difference in total cost-sharing expense for any drugs on a particular tier [50, 51].

Avalere Health, an advisory group focused on solving challenges facing the healthcare industry, estimated the impact of US legislation, PATA (H.R. 460), on commercial health plan premiums and cost-sharing strategies. It was estimated that there would be an approximately $US3.00 annual increase in premiums for individuals on plans with a specialty tier as well as a negligible $US0.37 average annual increase for those plans with a co-payment model and a $US7.78 average annual increase for those plans that implement co-insurance. Avalere Health concluded that the overall cost burden to commercial enrollees due to H.R. 460 will be minimal [52, 53]. Since the utilization of specialty pharmaceuticals is relatively inelastic, decreases in cost sharing for these medications will result in an estimated 3 % increase in specialty drug spend [54].

3 Looking Forward: The Future and Identification of Gaps in Specialty Pharmaceutical Cost Management

On a global scale, there will continue to be a rise in specialty pharmaceutical penetration of the market, with between 600 and 1,000 specialty drugs in the global pipeline according to Chief Financial Officer Jeffrey L. Hall at the UBS Global Healthcare Conference. Global spending on medicines will grow to nearly $US1.2 trillion by 2016, with emerging markets, contributing to a greater share of spending, particularly for biologics, and generic medications. Of this spending, an estimated $US200–210 billion is expected for spending on biologic medications, with $US4–6 billion (2 % of biologic spending) toward biosimilars [7, 35–57].

In the US, forecasts indicate that specialty drug spend will increase about 20 % annually and consume 40 % of the drug budget by 2016. Across the US healthcare industry, there are growing concerns about the high costs of specialty drugs. Changes in prescription benefit design, and utilization of cost-management strategies, will continue to evolve in order to ensure value-based healthcare decisions for specialty pharmaceuticals [13]. However, gaps in data exist regarding the utilization and cost management of specialty pharmaceuticals, particularly on a global scale.

Specialty pharmaceuticals are a rapidly growing and dynamic component of the healthcare industry and pharmaceutical market; with this comes greater clinical utilization as well as increased costs. Since significant differences exist between traditional pharmaceuticals and specialty pharmaceuticals, all involved stakeholders, including payers and providers, have adjusted current techniques and implemented innovative strategies to ensure appropriate drug utilization and management. However, these trends have evolved over the last decade and will continue to progress with advances in specialty pharmaceutical development and utilization as well as healthcare reform practices.

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